1: J Pept Sci. 2002 Apr;8(4):144-50. Related Article

Identification of single amino acid residues essential for the bind of lipopolysaccharide (LPS) to LPS binding protein (LBP) resid 86-99 by using an Ala-scanning library.

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Lipopolysaccharide binding protein (LBP) is a 60 kDa acute phase glycoprot capable of binding to LPS of Gram-negative bacteria and facilitating its inter with cellular receptors. This process is thought to be of great importance in systemic inflammatory reactions such as septic shock. A peptide correspondi residues 86-99 of human LBP (LBP86-99) has been reported to bind specific with high affinity the lipid A moiety of LPS and to inhibit the interaction of l with LBP. We identified essential amino acids in LBP86-99 for binding to L using a peptide library corresponding to the Ala-scanning of human LBP resi 86-99. Amino acids Trp91 and Lys92 were indispensable for peptide-LPS interaction and inhibition of LBP-LPS binding. In addition, several alanine-substituted synthetic LBP-derived peptides inhibited LPS-LBP interaction. Substitution of amino acids Arg94, Lys95 and Phe98 by Ala increased the inhibitory effect. The mutant Lys95 was the most active in blocking LPS bin to LBP. These findings emphasize the importance of single amino acids in th binding capacity of small peptides and may contribute to the development of drugs for use in the treatment of Gram-negative bacterial sepsis.

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☐ 1: J Endotoxin Res. 2003;9(5):281-91. Related Article

Inhibition of LPS-responses by synthetic peptides derived from associates with the ability of the peptides to block LBP-LPS interaction.

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The ability of LPS-binding protein (LBP) to greatly potentiate cell responses lipopolysaccharide (LPS) may largely contribute to LPS toxicity in sepsis. Tl study of agents with the capacity to block the interaction between LBP and L might improve the understanding of the role of LBP in Gram-negative infecti as well as offering new therapeutic tools for septic disorders. Here we confirı ability of synthetic peptides comprising the human LBP amino acid region 8(to interfere with the LBP-LPS interaction. The analysis of selected alanine m of a blocking peptide corresponding to the LBP region 86-99 suggests the importance of peptide amphipathicity for the inhibitory activity. The potency the native peptide and a selected analogue at inhibiting in vitro and in vivo L induced responses was associated with their relative activity in blocking LBF interaction. It was remarkable that these peptides were at least 500-fold more active in vivo than in vitro. Also, the inhibitory activity of peptides LBP86-9 LBPK95A seems to be independent of LBP concentrations, a behavior that n relevant for the potential use of these peptides in septic disorders where LBP serum concentrations are considerably elevated.

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